REMARKS

Claims 1-11, 13-19 and 21-28 are pending in the present application. Claim 19 is canceled herein without prejudice to Applicant's right to prosecute the subject matter of this claim in a related application. Upon entry of the present Amendment, claims 1-11, 13-18 and 21-28 will be pending. As this Amendment reduces the total number of claims, and places the Application in condition for allowance or, at a minimum, reduces the outstanding issues for appeal, Applicant asserts that entry of this Amendment is proper, and respectfully requests that the Amendment be entered and considered.

The Double Patenting Rejections

The Examiner has provisionally rejected claims 1-11, 13-19 and 21-28 under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 20, 21, 25-28, 34-47, 50, 54, 57, 58 and 62-82 of copending application no. 10/366,671 ("the '671 application"). Applicant requests that this rejection be held in abeyance until such time as one set of claims is deemed allowable.

The Rejection Under 35 U.S.C. 103(a) Should Be Withdrawn

The Examiner has rejected claims 1-11, 13-19 and 21-28 under 35 U.S.C. § 103(a) as obvious over Boyse in light of Kondo, Sakabe *et al.* ("Sakabe"), Gluckman *et al.* (1998) ("Gluckman (1998)") and Gluckman *et al.* (2001) ("Gluckman (2001)"). Sakabe is cited only as evidence that blood stem cells comprise $CD34^+CD38^+$ cells and $CD34^+CD38^-$ cells. Office Action at page 4. Kondo is cited only to show that blood comprises growth factors. Office Action at page 4. Claim 19 is canceled herein. Applicant respectfully traverses this rejection.

To establish a *prima facie* case of obviousness, the Examiner must demonstrate three things with respect to each claim: (1) the cited references, when combined, teach or suggest every element of the claim; (2) one of ordinary skill would have been motivated to combine the teachings of the cited references at the time of the invention; and (3) there would have been a reasonable expectation that the claimed invention would succeed. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

Acknowledging that Boyse does not teach or suggest the administration of over 5 billion nucleated cells, the Examiner cites Gluckman (1998), which the Examiner argues teaches the administration of a "high number" of nucleated cells. Office Action at page 4. Gluckman (1998), however does not broadly teach that *any* "high number" of transplanted nucleated cells is desirable. Rather, the "high number" of total nucleated cells taught by

Gluckman (1998) is only a number above the median number of such cells, 11 x 10^8, in a unit of cord blood (page 9, right column), a number that is almost an order of magnitude *less* than the number of total nucleated cells required in the currently-pending claims. Gluckman (1998) also teaches that the most nucleated cells obtained from a single unit of cord blood was 58 x 10^8 (page 9, right column), which is effectively the upper limit of the number of administrable nucleoated cells taught by Gluckman (1998). Moreover, Gluckman (1998) fails to suggest administration of more than the cells from a single unit of cord blood. As such, Gluckman (1998) fails to teach or suggest, missing in Boyse, of administration of as many as 1 x 10^{10}, or more, total nucleated cells.

The Examiner contends that one of ordinary skill in the art "would be further motivated to use cord blood cells that are not a perfect HLA type match for the expected benefit of increasing the number of available cells per transfusion by pooling together cord blood from several donors," Office Action at page 5, by, for example, "repeating the administration of Gluckman et al. (1998) 20 times." Office action at page 6. Such pooling, however, is not taught or suggested by either Gluckman (1998) or Gluckman (2001). Indeed, Gluckman (1998), merely suggests pooling as an "avenue of research." (*see* page 10, right column, first paragraph), and the later Gluckman reference, Gluckman (2001), is completely silent regarding pooling, focusing only on single units.

The Examiner also argues that one of ordinary skill in the art would have been motivated to pool, or to repeat administrations until a particular number of nucleated cells had been administered, in part, because "Gluckman et al. (2001) teach that [HLA] typing is not a major factor for selecting a cord blood donor." Office Action at page 5; *see* page 6. However, Gluckman (2001) reports that GVHD is a significant factor to consider with respect to administration of even a single unit of cord blood. For example, Gluckman (2001) states that a full 21% of unmatched, single-unit cord blood recipients experienced acute Grade II or IV graft-versus-host disease. (*See* Gluckman (2001) at page 153, left column, third paragraph.) Neither Gluckman (1998) nor Gluckman (2001) teach or suggest that pooled cord blood units, which would comprise cells from two or more antigenically distinct donors, would be tolerated by a recipient to the same degree as a single unit. Rather, especially in view of the results presented in Gluckman (2001), one of ordinary skill would want to *minimize* the sources of antigenically distinct material being administered. Certainly, neither Gluckman (1998) nor Gluckman (2001) teaches or suggests that administrations of cord blood from 20 different donors, as suggested by the Examiner (Office Action, page 6), would be tolerated by a recipient.

Moreover, in view of the amount of GVHD observed, the Examiner's assertions that the "skilled artisan would be motivated to attempt a transfusion with as many cells as possible," Office Action at page 5, and that administration of 10 billion or more nucleated cells is a matter of "routine optimization," clearly constitute an obvious to *try* basis of rejection, which is not sufficient for an obviousness rejection. *See, e.g., in re Roemer*, 258 F.3d 1303 (Fed. Cir. 2001).

Because, Gluckman (1998), Gluckman (2001) and Boyse, individually and in combination, teach or suggest administration of only substantially lower numbers of cells per kilogram than is claimed in the present invention (*see, e.g.*, specification, page 27, lines 8-11), particularly given that both Gluckman references only teach the administration of single units of cord blood, which would naturally limit the number of cells administered, and because at least Gluckman (2001) demonstrates that administration of single units of cord blood risks initiating GVHD, administration of higher numbers of nucleated cells is not routine. Moreover, none of the cited references teaches or suggests the administration of a particular number of *stem cells* from cord blood, and provides no guidance as to the number to administer or the risks involved in such administration. As a result, "optimization" of the number of stem cells to achieve an administration of 1 billion is not routine.

Sakabe and Kondo also fail to supply the teachings missing in the combination of Boyse, Gluckman (1998) and Gluckman (2001). In particular, as pointed out above, Kondo merely shows that blood comprises growth factors, and Sakabe merely shows that blood stem cells contain $CD34^+CD38^+$ $CD34^+CD38^-$ cells. For the above reasons, therefore, the combination of Gluckman (1998) and Gluckman (2001) with Boyse, Sakabe and Kondo, does not teach or suggest the administration of 1×10^{10} nucleated cells, or 1×10^9 stem cells, as claimed in the present invention.

Applicant also traverses the rejection of claims 10 and 14-23 as obvious over the cited references. At the outset, Applicant points out that the cited references, as discussed above, do not teach or suggest administration of 1×10^{10} nucleated cells or 1×10^9 stem cells, as recited in the rejected claims. In addition, with respect, the Examiner has misapplied the principles of inherency in making this rejection, because treatment of myelodysplasia, or the conditions of claims 14-18 and 20-23, are not necessary outcomes of administering cord blood. "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990).

The Examiner admits that "Boyse et al. do not teach treating myelodysplasia or treating patients with the specific conditions recited in claims 14-23." Office Action at page 4. However, the Examiner argues that Boyse performs the same administration of cord blood cells as in the present application, and, because the method step of Boyse (administration of cord blood) is the same as the instantly claimed step, Boyse inherently teaches the same process of treatment of myelodysplasia and treatment of patients diagnosed with various disorders as in the current application. *Id.*

Boyse does not, however, inherently teach the treatment of the conditions recited in claims 10, 14-18 or 20-23 because persons of ordinary skill in the art, following the teachings of Boyse, would not necessarily and always treat each of such conditions. For example, treatment of, *e.g.*, myelodysplasia according to claim 10, is not an inherent aspect of administering cord blood to an individual, because it is entirely possible to administer cord blood to a person who does not have myelodysplasia. The fact that a certain result or characteristic *may* occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (court reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). Thus, treatment of myelodysplasia is not a necessary, or inherent, outcome of administration of cord blood by the method of Boyse. By the same logic, Boyse does not inherently teach the treatment of any of the other conditions recited in claims 14-18 or 20-23.

The issue is not whether cord blood, if administered according to the teaching of Boyse to a person having, *e.g.*, myelodysplasia, would treat the myelodysplasia. Rather, the issue is whether Boyse teaches or suggests the treatment of myelodysplasia *per se*, or any of the other particularly recited disorders. It does not. *Compare Perricone v. Medicis Pharmaceutical Corp.*, 432 F.3d 1368, 1378 (Fed. Cir. 2006) ("The issue is not, as the dissent and district court imply, whether Pereira's lotion *if applied* to skin sunburn would inherently treat that damage, but whether Pereira discloses the application of its composition to skin sunburn. It does not.").

Because Boyse does not inherently teach the administration of cord blood wherein the recipient has myelodysplasia, or any of the other conditions recited in claims 14-18 or 20-23, and because none of the other references remedy this deficiency, the cited combination of references fails to teach administration of cord blood according to claims 10, 14-18 or 20-23. Applicant therefore respectfully requests that the Examiner remove this rejection on this basis.

Given the above, Applicant submits that the combination of Boyse, Sakabe, Kondo, Gluckman (1998) and Gluckman (2001) does not render any of claims 1-11, 13-18 and 20-28 obvious. Applicant respectfully requests that the Examiner withdraw the rejection of claims 1-11, 13-18 and 20-28 on this basis.

Conclusion

For the reasons provided above, the claims should now be in condition for allowance, and early notice of the same is earnestly solicited. No new search of the prior art is required to assess patentabilty of the claims. Applicant believes that no fee is due for this Amendment, beyond that authorized in the accompanying documents. However, if a fee should be deemed due, please charge such fee to Jones Day deposit account no. 50-3013.

Respectfully submitted,

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